

## CLAIMS

1. A method of diagnosing or prognosticating Alzheimer's disease in a subject, or determining whether a subject is at increased risk of developing said disease,  
5 comprising determining a level and/or an activity of
  - (i) a transcription product of a gene coding for SGPL1, and/or
  - (ii) a translation product of a gene coding for SGPL1, and/or
  - (iii) a fragment, or derivative, or variant of said transcription or translation product,
- 10 in a sample obtained from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.
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2. A kit for diagnosing or prognosticating Alzheimer's disease in a subject, or determining the propensity or predisposition of a subject to develop such a disease, said kit comprising:
  - (a) at least one reagent which is selected from the group consisting of (i) reagents  
20 that selectively detect a transcription product of a gene coding for SGPL1 and (ii) reagents that selectively detect a translation product of a gene coding for SGPL1;whereby the diagnosis or prognosis or determination of the propensity or predisposition to develop Alzheimer's disease is determined by the steps of (i)  
25 detecting in a sample obtained from said subject a level, or an activity, or both said level and said activity of a transcription product and/or of a translation product of a gene coding for SGPL1, and (ii) comparing said level or activity, or both said level and said activity of a transcription product and/or of a translation product of a gene coding for SGPL1 to a reference value representing a known health status and/or  
30 to a reference value representing a known disease status, and said level, or activity, or both said level and said activity, of said transcription product and/or said translation product is varied compared to a reference value representing a known health status, and/or is similar or equal to a reference value representing a known disease status.

3. A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of

- (i) a gene coding for SGPL1, and/or
- (ii) a transcription product of a gene coding for SGPL1, and/or
- 5 (iii) a translation product of a gene coding for SGPL1, and/or
- (iv) a fragment, or derivative, or variant of (i) to (iii).

4. A recombinant, genetically altered non-human animal comprising a non-native gene sequence coding for SGPL1 or a fragment, or a derivative, or a variant 10 thereof, said animal being obtainable by:

- (i) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and
- (ii) introducing said targeting construct into a stem cell of a non-human animal, and
- 15 (iii) introducing said non-human animal stem cell into a non-human embryo, and
- (iv) transplanting said embryo into a pseudopregnant non-human animal, and
- (v) allowing said embryo to develop to term, and
- (vi) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and
- 20 (vii) breeding the genetically altered non-human animal of step (vi) to obtain a genetically altered non-human animal whose genome comprises a modification of said endogenous gene, wherein said disruption results in said non-human animal exhibiting a predisposition to developing symptoms of a neurodegenerative disease or related diseases or disorders, preferably symptoms similar to Alzheimer's disease.

25 5. Use of the recombinant, genetically altered non-human animal according to claim 4 for screening, testing, and validating compounds, agents, and modulators in the development of diagnostics and therapeutics to treat neurodegenerative 30 diseases, in particular Alzheimer's disease.

6. An assay for screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

- 35 (i) a gene coding for SGPL1, and/or
- (ii) a transcription product of a gene coding for SGPL1, and/or

(iii) a translation product of a gene coding for SGPL1, and/or  
(iv) a fragment, or derivative, or variant of (i) to (iii),  
said method comprising:  
(a) contacting a cell with a test compound;  
5 (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);  
(c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and  
(d) comparing the levels and/or activities of the substance in the cells of step  
10 (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.

7. A method of screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of  
15 (i) a gene coding for SGPL1, and/or  
(ii) a transcription product of a gene coding for SGPL1, and/or  
(iii) a translation product of a gene coding for SGPL1, and/or  
20 (v) a fragment, or derivative, or variant of (i) to (iii),  
said method comprising:  
(a) administering a test compound to a non-human test animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv);  
25 (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);  
(c) measuring the activity and/or level of one or more substances recited in (i) or (iv) in a matched non-human control animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect to the substances recited in (i) to (iv) and to which animal no such test compound has been administered;  
30 (d) comparing the activity and/or level of the substance in the animals of step (b) and (c), wherein an alteration in the activity and/or level of substances in  
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the non-human test animal indicates that the test compound is a modulator of said diseases or disorders.

8. The method according to claim 7 wherein said non-human test animal and/or

5 said control animal is a recombinant, genetically altered animal which expresses the gene coding for SGPL1, or a fragment, or a derivative, or a variant thereof, under the control of a transcriptional control element which is not the native SGPL1 gene transcriptional control element.

10 9. An assay for testing a compound, preferably for screening a plurality of compounds to determine the degree of binding of said compounds to a SGPL1 translation product, or to a fragment, or derivative, or variant thereof, said assay comprising the steps of:

(i) adding a liquid suspension of said SGPL1 translation product, or a fragment, or derivative, or variant thereof, to a plurality of containers;

15 (ii) adding a detectable, in particular a fluorescently labelled compound or a plurality of fluorescently labelled compounds to be screened for said binding to said plurality of containers;

(iii) incubating said SGPL1 translation product, or said fragment, or derivative, or variant thereof, and said detectable, in particular fluorescently labelled compound or fluorescently labelled compounds;

20 (iv) measuring amounts of preferably fluorescence associated with said SGPL1 translation product, or with said fragment, or derivative, or variant thereof; and

25 (v) determining the degree of binding by one or more of said compounds to said SGPL1 translation product, or said fragment, or derivative, or variant thereof.

10. Use of a protein molecule of SEQ ID NO. 1, said protein molecule being a

30 translation product of the gene coding for SGPL1, or a fragment, or derivative, or variant thereof, as diagnostic target for detecting Alzheimer's disease.

11. Use of a protein molecule of SEQ ID NO. 1, said protein molecule being a

35 translation product of the gene coding for SGPL1, or a fragment, or derivative, or variant thereof, as screening target for reagents or compounds preventing, or treating, or ameliorating Alzheimer's disease.

12. Use of an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of a gene coding for SGPL1, SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for detecting a pathological state 5 of a cell in a sample obtained from a subject, comprising immunocytochemical staining of said cell with said antibody, wherein an altered degree of staining or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell which relates to a neurodegenerative disease, preferably to Alzheimer's disease.